## **AMENDMENT**

## **Amendments to the Claims:**

Please cancel claims 27, 28, 52, 54-60, 62, 63, 65-71, 73, 74, 76-85, 87, 88, 90, 91, 93, 95-100, and 102-111 without prejudice and amend claims 5, 12, 15, 16, 19-23, 30-32, 35-38, 46, 65, 67, and 69 as shown.

The following listing of claims supersedes all prior versions and listings of claims in the application:

## **Listing of Claims:**

- 1. (Original) An isolated nucleic acid having a nucleotide sequence selected from the group consisting of:
  - (a) at least 10 consecutive nucleotides of SEQ ID NO: 1;
  - (b) at least 12 consecutive nucleotides of SEQ ID NO: 1;
  - (c) at least 14 consecutive nucleotides of SEQ ID NO: 1;
  - (d) at least 16 consecutive nucleotides of SEQ ID NO: 1;
  - (e) at least 18 consecutive nucleotides of SEQ ID NO: 1; and
  - (f) a sequence complementary to any one of the sequences of (a) –(e).
- 2. (Original) An isolated nucleic acid having a nucleotide sequence selected from the group consisting of:
  - (a) at least 10 consecutive nucleotides of SEQ ID NO: 3;
  - (b) at least 12 consecutive nucleotides of SEQ ID NO: 3;
  - (c) at least 14 consecutive nucleotides of SEQ ID NO: 3;
  - (d) at least 16 consecutive nucleotides of SEQ ID NO: 3;
  - (e) at least 18 consecutive nucleotides of SEQ ID NO: 3; and
  - (f) a sequence complementary to any one of the sequences of (a) –(e).

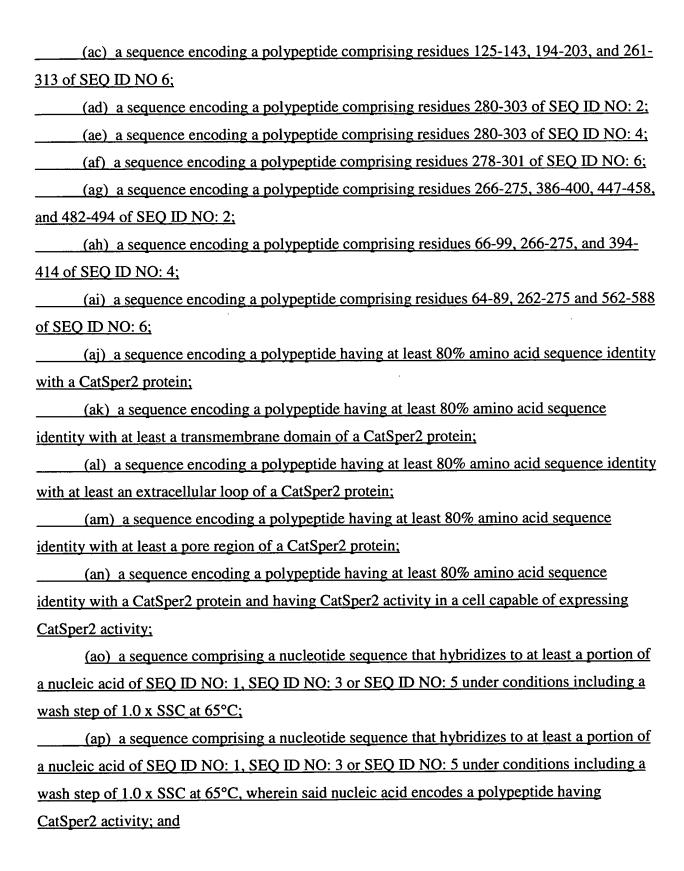
- 3. (Original) An isolated nucleic acid having a nucleotide sequence selected from the group consisting of:
  - (a) at least 10 consecutive nucleotides of SEQ ID NO: 5;
  - (b) at least 12 consecutive nucleotides of SEQ ID NO: 5;
  - (c) at least 14 consecutive nucleotides of SEQ ID NO: 5;
  - (d) at least 16 consecutive nucleotides of SEQ ID NO: 5;
  - (e) at least 18 consecutive nucleotides of SEQ ID NO: 5; and
  - (f) a sequence complementary to any one of the sequences of (a) –(e).
- 4. (Original) An isolated nucleic acid having a nucleotide sequence selected from the group consisting of:
  - (a) a sequence encoding a CatSper2 protein;
  - (b) a sequence encoding at least a transmembrane domain of a CatSper2 protein;
  - (c) a sequence encoding at least an extracellular loop of a CatSper2 protein;
  - (d) a sequence encoding at least a pore region of a CatSper2 protein;
- (e) a sequence encoding at least an epitope of a CatSper2 protein having high predicted antigenicity; and
  - (f) a sequence complementary to any one of the sequences of (a)–(e).
- 5. (Currently amended) An isolated nucleic acid as in claim [[43]] 4 selected from the group consisting of:
  - (a) a sequence encoding SEQ ID NO: 2;
  - (b) a sequence encoding SEQ ID NO: 4;
  - (c) a sequence encoding SEQ ID NO: 6;
- (d) a sequence encoding a polypeptide comprising residues 104-126, 146-166, 176-195, 206-228, 241-262, and 316-340 of SEQ ID NO: 2;
- (e) a sequence encoding a polypeptide comprising residues 104-126, 146-166, 176-195, 206-228, 241-262, and 316-340 of SEQ ID NO: 4;

- (f) a sequence encoding a polypeptide comprising residues 102-124, 144-164, 174-193, 204-227, 239-260, and 314-338 of SEQ ID NO: 6;
- (g) a sequence encoding a polypeptide comprising residues 127-145, 196-205, and 263-315 of SEQ ID NO: 2;
- (h) a sequence encoding a polypeptide comprising residues 127-145, 196-205, and 265-315 of SEQ ID NO 4;
- (i) a sequence encoding a polypeptide comprising residues 125-143, 194-203, and 261-313 of SEQ ID NO 6;
  - (j) a sequence encoding a polypeptide comprising residues 280-303 of SEQ ID NO: 2;
  - (k) a sequence encoding a polypeptide comprising residues 280-303 of SEQ ID NO: 4;
  - (1) a sequence encoding a polypeptide comprising residues 278-301 of SEQ ID NO: 6;
- (m) a sequence encoding a polypeptide comprising residues 266-275, 386-400, 447-458, and 482-494 of SEQ ID NO: 2;
- (n) a sequence encoding a polypeptide comprising residues 66-99, 266-275, and 394-414 of SEQ ID NO: 4;
- (o) a sequence encoding a polypeptide comprising residues 64-89, 262-275 and 562-588 of SEQ ID NO: 6; and
  - (p) a sequence complementary to any one of the sequences of (a)–(o).
- 6. (Original) An isolated nucleic acid encoding a polypeptide having at least 80% amino acid sequence identity with a polypeptide selected from the group consisting of:
  - (a) a CatSper2 protein;
  - (b) at least a transmembrane domain of a CatSper2 protein;
  - (c) at least an extracellular loop of a CatSper2 protein; and
  - (d) at least a pore region of a CatSper2 protein.
- 7. (Original) An isolated nucleic acid encoding a polypeptide having at least 80% amino acid sequence identity with a CatSper2 protein and having CatSper2 activity in a cell capable of expressing CatSper2 activity.

- 8. (Original) An isolated nucleic acid comprising a nucleotide sequence that hybridizes to at least a portion of a nucleic acid of SEQ ID NO: 1, SEQ ID NO: 3 or SEQ ID NO: 5 under conditions including a wash step of 1.0 x SSC at 65°C.
- 9. (Original) An isolated nucleic acid as in claim 8 wherein said nucleic acid encodes a polypeptide having CatSper2 activity.
- 10. (Original) A nucleic acid comprising:
- (i) a nucleotide sequence encoding a polypeptide having CatSper2 activity, wherein said nucleic acid hybridizes to at least a portion of a nucleic acid of SEQ ID NO: 1, SEQ ID NO: 3 or SEO ID NO: 5 under conditions including a wash step of 1.0 x SSC at 65°C; and
- (ii) a heterologous regulatory region operably joined to said sequence such that said sequence is expressed.
- 11. (Original) A nucleic acid comprising:
- (i) a nucleotide sequence encoding a polypeptide having at least 80% amino acid sequence identity with an amino acid sequence of SEQ ID NO: 2, SEQ ID NO: 4 or SEQ ID NO: 6; and
- (ii) a heterologous regulatory region operably joined to said sequence such that said sequence is expressed.
- 12. (Currently amended) A kit for detecting at least a portion of a CatSper2 nucleic acid comprising an isolated nucleic acid of any one of claims 1-7 and a means for detecting said isolated nucleic acid, wherein the isolated nucleic acid is selected from the group consisting of

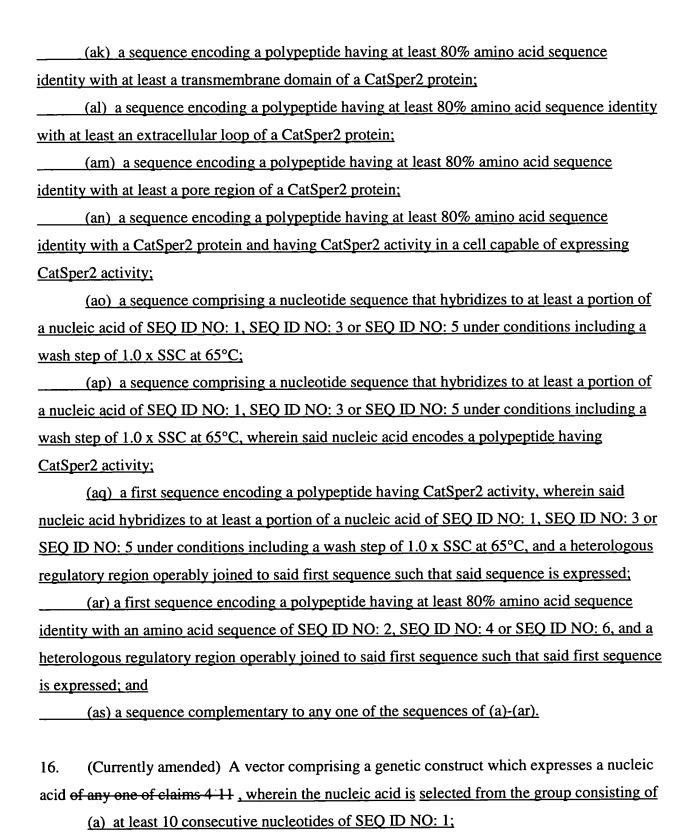
  (a) at least 10 consecutive nucleotides of SEQ ID NO: 1;
  (b) at least 12 consecutive nucleotides of SEQ ID NO: 1;
  - (c) at least 14 consecutive nucleotides of SEQ ID NO: 1;
    - (d) at least 16 consecutive nucleotides of SEQ ID NO: 1;
  - (e) at least 18 consecutive nucleotides of SEQ ID NO: 1;

(f) at least 10 consecutive nucleotides of SEQ ID NO: 3;
(g) at least 12 consecutive nucleotides of SEQ ID NO: 3;
(h) at least 14 consecutive nucleotides of SEQ ID NO: 3;
(i) at least 16 consecutive nucleotides of SEQ ID NO: 3;
(j) at least 18 consecutive nucleotides of SEQ ID NO: 3;
(k) at least 10 consecutive nucleotides of SEQ ID NO: 5;
(1) at least 12 consecutive nucleotides of SEQ ID NO: 5;
(m) at least 14 consecutive nucleotides of SEQ ID NO: 5;
(n) at least 16 consecutive nucleotides of SEQ ID NO: 5;
(o) at least 18 consecutive nucleotides of SEQ ID NO: 5;
(p) a sequence encoding a CatSper2 protein;
(q) a sequence encoding at least a transmembrane domain of a CatSper2 protein;
(r) a sequence encoding at least an extracellular loop of a CatSper2 protein;
(s) a sequence encoding at least a pore region of a CatSper2 protein;
(t) a sequence encoding at least an epitope of a CatSper2 protein having high predicted
antigenicity;
(u) a sequence encoding SEQ ID NO: 2;
(v) a sequence encoding SEQ ID NO: 4;
(w) a sequence encoding SEQ ID NO: 6;
(x) a sequence encoding a polypeptide comprising residues 104-126, 146-166, 176-195,
206-228, 241-262, and 316-340 of SEQ ID NO: 2;
(y) a sequence encoding a polypeptide comprising residues 104-126, 146-166, 176-195,
206-228, 241-262, and 316-340 of SEQ ID NO: 4;
(z) a sequence encoding a polypeptide comprising residues 102-124, 144-164, 174-193,
204-227, 239-260, and 314-338 of SEQ ID NO: 6;
(aa) a sequence encoding a polypeptide comprising residues 127-145, 196-205, and 263-
315 of SEQ ID NO: 2; (ab) a sequence encoding a polypeptide comprising residues 127-145, 196-205, and 265-
315 of SEQ ID NO 4;

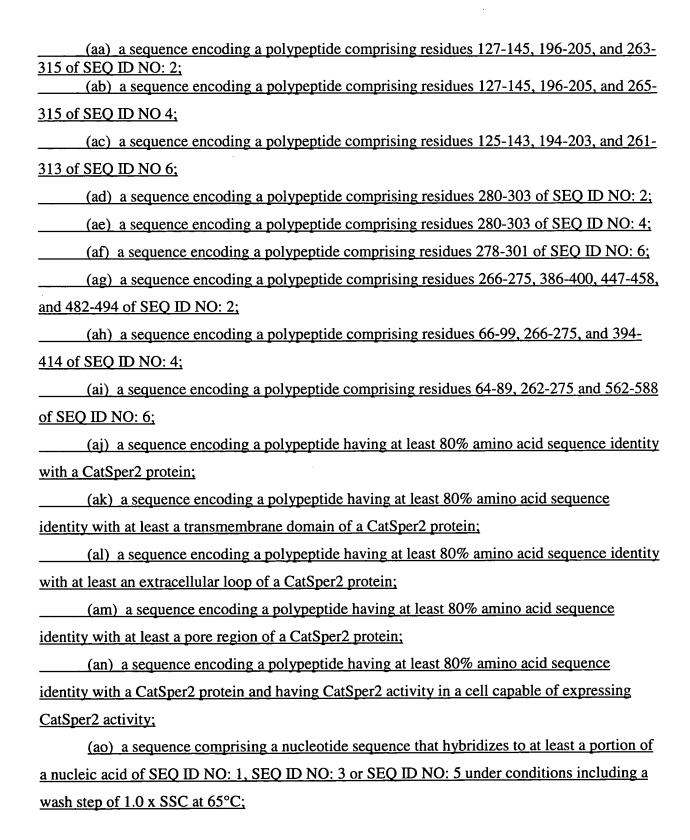


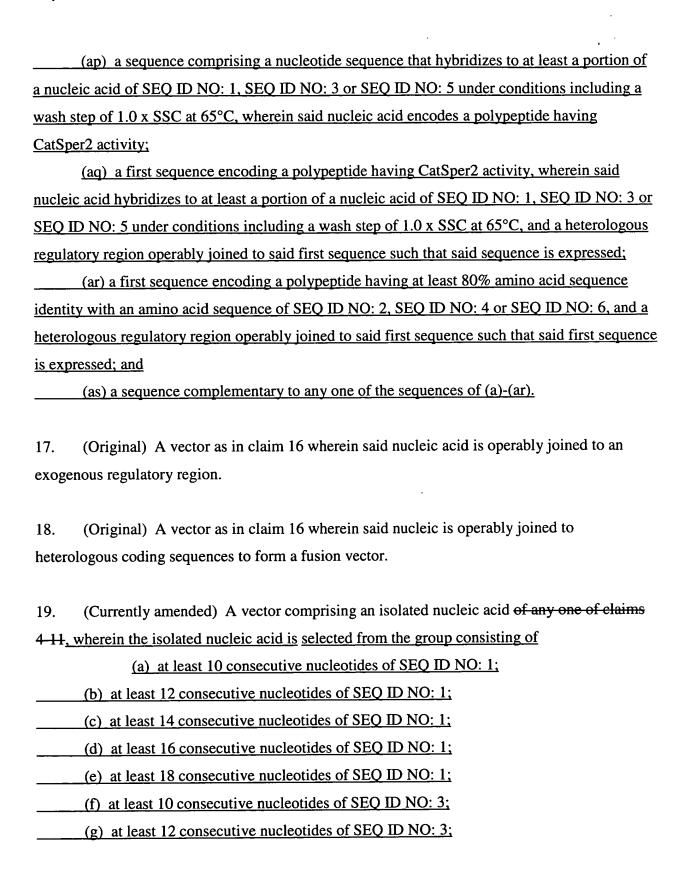
	(aq) a sequence complementary to any one of the sequences of (a)-(ap).
13.	(Original) A kit as in claim 12 wherein said means for detecting said isolated nucleic
acid co	omprises a detectable label bound thereto.
14.	(Original) A kit as in claim 12 wherein said means for detecting said isolated nucleic
acid co	omprises a labeled secondary nucleic acid which specifically hybridizes to said isolated
nuclei	c acid.
15.	(Currently amended) A vector comprising an isolated nucleic acid of any one of claims
<del>1 11</del> <u>.</u>	wherein the isolated nucleic acid is selected from the group consisting of
	(a) at least 10 consecutive nucleotides of SEQ ID NO: 1;
	(b) at least 12 consecutive nucleotides of SEQ ID NO: 1;
	(c) at least 14 consecutive nucleotides of SEQ ID NO: 1;
<del></del>	(d) at least 16 consecutive nucleotides of SEQ ID NO: 1;
	(e) at least 18 consecutive nucleotides of SEQ ID NO: 1;
	(f) at least 10 consecutive nucleotides of SEQ ID NO: 3;
	(g) at least 12 consecutive nucleotides of SEQ ID NO: 3;
	(h) at least 14 consecutive nucleotides of SEQ ID NO: 3;
	(i) at least 16 consecutive nucleotides of SEQ ID NO: 3;
	(j) at least 18 consecutive nucleotides of SEQ ID NO: 3;
	(k) at least 10 consecutive nucleotides of SEQ ID NO: 5;
	(I) at least 12 consecutive nucleotides of SEQ ID NO: 5;
	(m) at least 14 consecutive nucleotides of SEQ ID NO: 5;
	(n) at least 16 consecutive nucleotides of SEQ ID NO: 5;
	(o) at least 18 consecutive nucleotides of SEQ ID NO: 5;
	(p) a sequence encoding a CatSper2 protein;
	(q) a sequence encoding at least a transmembrane domain of a CatSper2 protein;
	(r) a sequence encoding at least an extracellular loop of a CatSper2 protein;

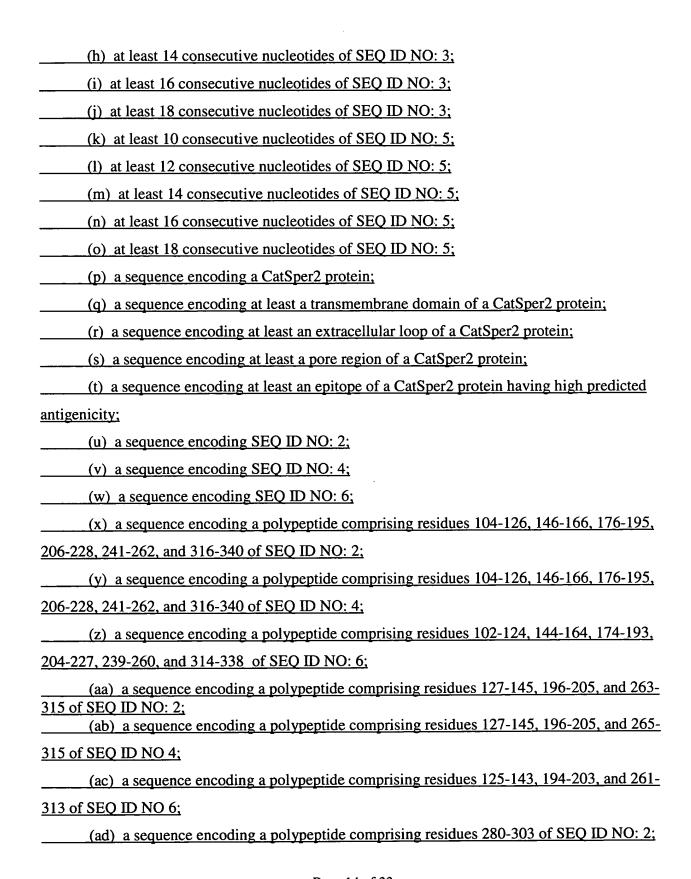
(s) a sequence encoding at least a pore region of a CatSper2 protein;
(t) a sequence encoding at least an epitope of a CatSper2 protein having high predicted
antigenicity;
(u) a sequence encoding SEQ ID NO: 2;
(v) a sequence encoding SEQ ID NO: 4;
(w) a sequence encoding SEQ ID NO: 6;
(x) a sequence encoding a polypeptide comprising residues 104-126, 146-166, 176-195,
206-228, 241-262, and 316-340 of SEQ ID NO: 2;
(y) a sequence encoding a polypeptide comprising residues 104-126, 146-166, 176-195,
206-228, 241-262, and 316-340 of SEQ ID NO: 4;
(z) a sequence encoding a polypeptide comprising residues 102-124, 144-164, 174-193,
204-227, 239-260, and 314-338 of SEQ ID NO: 6;
(aa) a sequence encoding a polypeptide comprising residues 127-145, 196-205, and 263-315 of SEQ ID NO: 2;
(ab) a sequence encoding a polypeptide comprising residues 127-145, 196-205, and 265-
315 of SEQ ID NO 4;
(ac) a sequence encoding a polypeptide comprising residues 125-143, 194-203, and 261-
313 of SEQ ID NO 6;
(ad) a sequence encoding a polypeptide comprising residues 280-303 of SEQ ID NO: 2;
(ae) a sequence encoding a polypeptide comprising residues 280-303 of SEQ ID NO: 4;
(af) a sequence encoding a polypeptide comprising residues 278-301 of SEQ ID NO: 6;
(ag) a sequence encoding a polypeptide comprising residues 266-275, 386-400, 447-458,
and 482-494 of SEQ ID NO: 2;
(ah) a sequence encoding a polypeptide comprising residues 66-99, 266-275, and 394-
414 of SEQ ID NO: 4;
(ai) a sequence encoding a polypeptide comprising residues 64-89, 262-275 and 562-588
of SEQ ID NO: 6;
(aj) a sequence encoding a polypeptide having at least 80% amino acid sequence identity
with a CatSper2 protein:

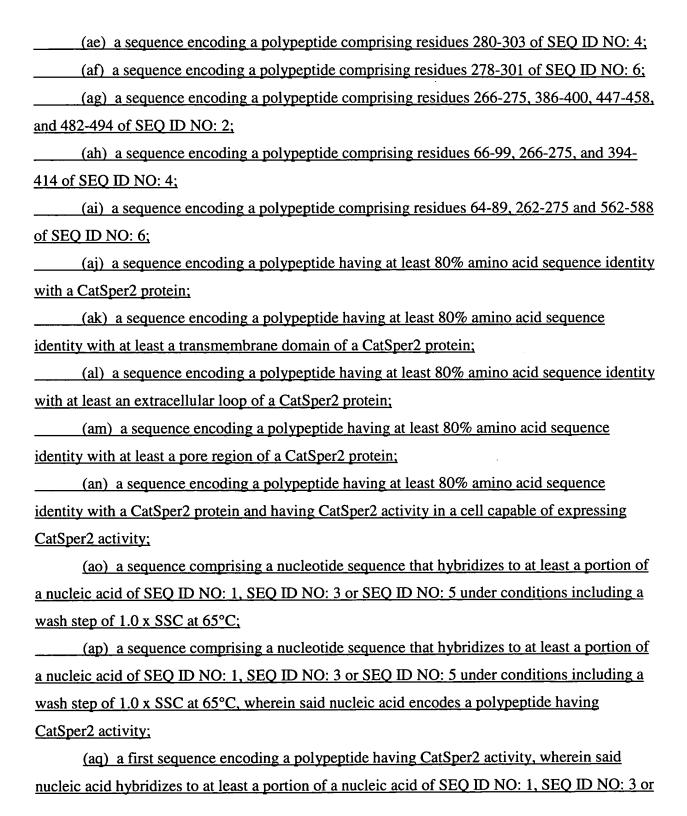


(b) at least 12 consecutive nucleotides of SEQ ID NO: 1;
(c) at least 14 consecutive nucleotides of SEQ ID NO: 1;
(d) at least 16 consecutive nucleotides of SEQ ID NO: 1;
(e) at least 18 consecutive nucleotides of SEQ ID NO: 1;
(f) at least 10 consecutive nucleotides of SEQ ID NO: 3;
(g) at least 12 consecutive nucleotides of SEQ ID NO: 3;
(h) at least 14 consecutive nucleotides of SEQ ID NO: 3;
(i) at least 16 consecutive nucleotides of SEQ ID NO: 3;
(j) at least 18 consecutive nucleotides of SEQ ID NO: 3;
(k) at least 10 consecutive nucleotides of SEQ ID NO: 5;
(1) at least 12 consecutive nucleotides of SEQ ID NO: 5;
(m) at least 14 consecutive nucleotides of SEQ ID NO: 5;
(n) at least 16 consecutive nucleotides of SEQ ID NO: 5;
(o) at least 18 consecutive nucleotides of SEQ ID NO: 5;
(p) a sequence encoding a CatSper2 protein;
(q) a sequence encoding at least a transmembrane domain of a CatSper2 protein;
(r) a sequence encoding at least an extracellular loop of a CatSper2 protein;
(s) a sequence encoding at least a pore region of a CatSper2 protein;
(t) a sequence encoding at least an epitope of a CatSper2 protein having high predicted
antigenicity;
(u) a sequence encoding SEQ ID NO: 2;
(v) a sequence encoding SEQ ID NO: 4;
(w) a sequence encoding SEQ ID NO: 6;
(x) a sequence encoding a polypeptide comprising residues 104-126, 146-166, 176-195
206-228, 241-262, and 316-340 of SEQ ID NO: 2;
(y) a sequence encoding a polypeptide comprising residues 104-126, 146-166, 176-195
206-228, 241-262, and 316-340 of SEQ ID NO: 4;
(z) a sequence encoding a polypeptide comprising residues 102-124, 144-164, 174-193
204-227, 239-260, and 314-338 of SEQ ID NO: 6;



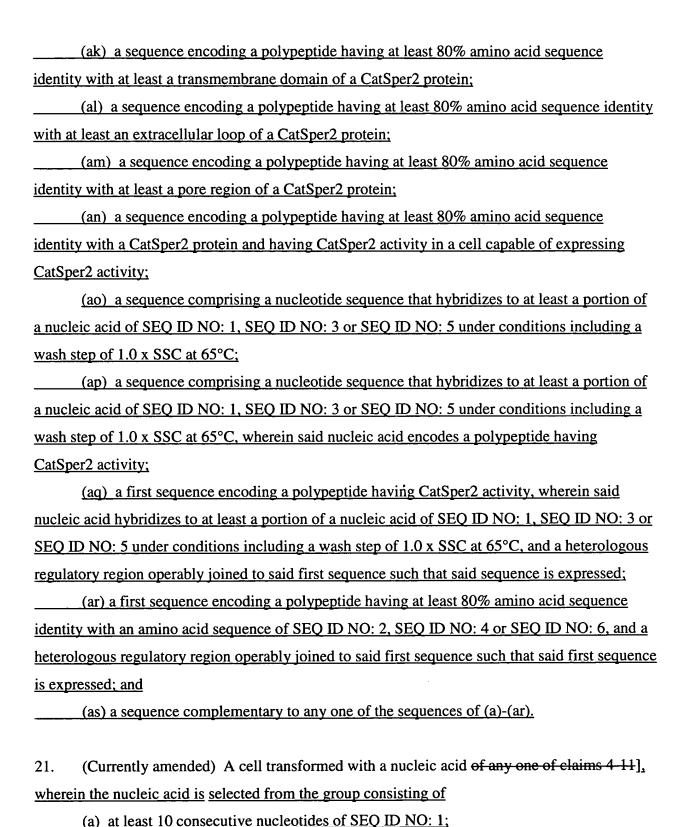




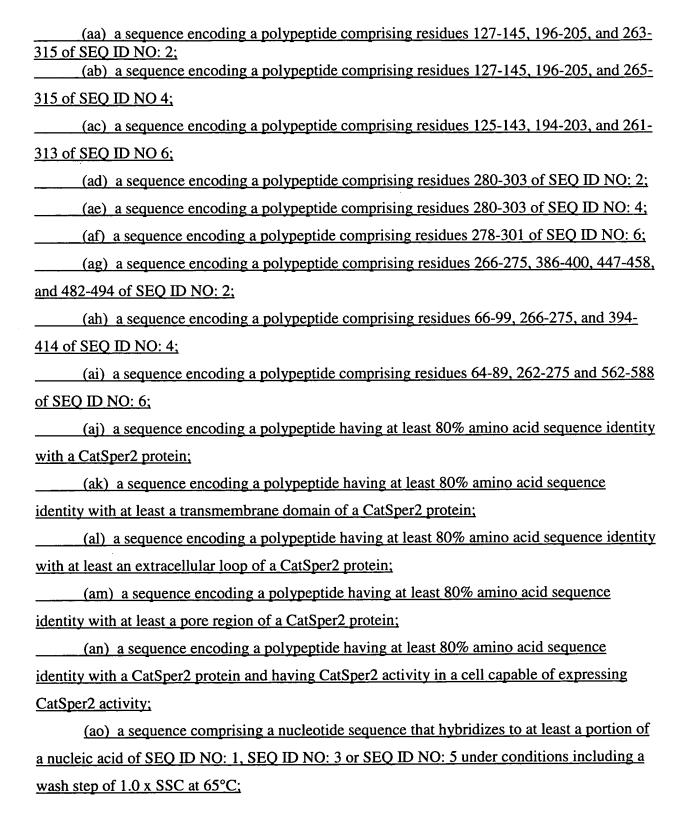


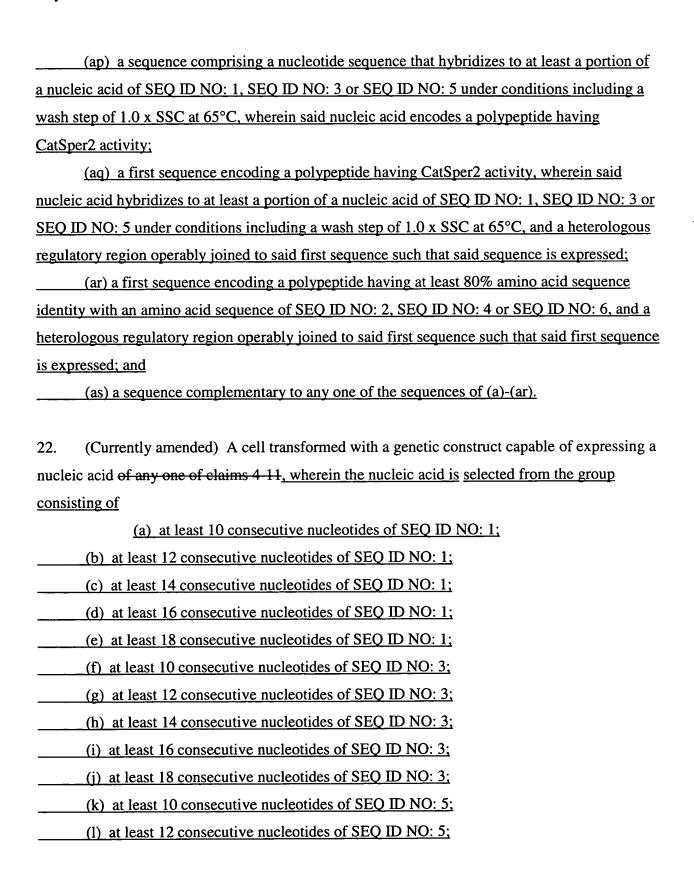
SEQ ID NO: 5 under conditions including a wash step of 1.0 x SSC at 65°C, and a heterologous
regulatory region operably joined to said first sequence such that said sequence is expressed;
(ar) a first sequence encoding a polypeptide having at least 80% amino acid sequence
identity with an amino acid sequence of SEQ ID NO: 2, SEQ ID NO: 4 or SEQ ID NO: 6, and a
heterologous regulatory region operably joined to said first sequence such that said first sequence
is expressed; and
(as) a sequence complementary to any one of the sequences of (a)-(ar).
20. (Currently amended) A vector comprising an isolated nucleic acid of any one of claims
4-11 operably joined to a reporter gene, wherein the isolated nucleic acid is selected from the
group consisting of
(a) at least 10 consecutive nucleotides of SEQ ID NO: 1;
(b) at least 12 consecutive nucleotides of SEQ ID NO: 1;
(c) at least 14 consecutive nucleotides of SEQ ID NO: 1;
(d) at least 16 consecutive nucleotides of SEQ ID NO: 1;
(e) at least 18 consecutive nucleotides of SEQ ID NO: 1;
(f) at least 10 consecutive nucleotides of SEQ ID NO: 3;
(g) at least 12 consecutive nucleotides of SEQ ID NO: 3;
(h) at least 14 consecutive nucleotides of SEQ ID NO: 3;
(i) at least 16 consecutive nucleotides of SEQ ID NO: 3;
(j) at least 18 consecutive nucleotides of SEQ ID NO: 3;
(k) at least 10 consecutive nucleotides of SEQ ID NO: 5;
(1) at least 12 consecutive nucleotides of SEQ ID NO: 5;
(m) at least 14 consecutive nucleotides of SEQ ID NO: 5;
(n) at least 16 consecutive nucleotides of SEQ ID NO: 5;
(o) at least 18 consecutive nucleotides of SEQ ID NO: 5;
(p) a sequence encoding a CatSper2 protein;
(q) a sequence encoding at least a transmembrane domain of a CatSper2 protein;
(r) a sequence encoding at least an extracellular loop of a CatSper2 protein:

(s) a sequence encoding at least a pore region of a CatSper2 protein;
(t) a sequence encoding at least an epitope of a CatSper2 protein having high predicted
antigenicity;
(u) a sequence encoding SEQ ID NO: 2;
(v) a sequence encoding SEQ ID NO: 4;
(w) a sequence encoding SEQ ID NO: 6;
(x) a sequence encoding a polypeptide comprising residues 104-126, 146-166, 176-195,
206-228, 241-262, and 316-340 of SEQ ID NO: 2;
(y) a sequence encoding a polypeptide comprising residues 104-126, 146-166, 176-195,
206-228, 241-262, and 316-340 of SEQ ID NO: 4;
(z) a sequence encoding a polypeptide comprising residues 102-124, 144-164, 174-193,
204-227, 239-260, and 314-338 of SEQ ID NO: 6;
(aa) a sequence encoding a polypeptide comprising residues 127-145, 196-205, and 263-315 of SEQ ID NO: 2;  (ab) a sequence encoding a polypeptide comprising residues 127-145, 196-205, and 265-
315 of SEQ ID NO 4;
(ac) a sequence encoding a polypeptide comprising residues 125-143, 194-203, and 261-
313 of SEQ ID NO 6;
(ad) a sequence encoding a polypeptide comprising residues 280-303 of SEQ ID NO: 2;
(ae) a sequence encoding a polypeptide comprising residues 280-303 of SEQ ID NO: 4;
(af) a sequence encoding a polypeptide comprising residues 278-301 of SEQ ID NO: 6;
(ag) a sequence encoding a polypeptide comprising residues 266-275, 386-400, 447-458,
and 482-494 of SEQ ID NO: 2;
(ah) a sequence encoding a polypeptide comprising residues 66-99, 266-275, and 394-
414 of SEQ ID NO: 4;
(ai) a sequence encoding a polypeptide comprising residues 64-89, 262-275 and 562-588
of SEQ ID NO: 6;
(aj) a sequence encoding a polypeptide having at least 80% amino acid sequence identity
with a CatSper2 protein:

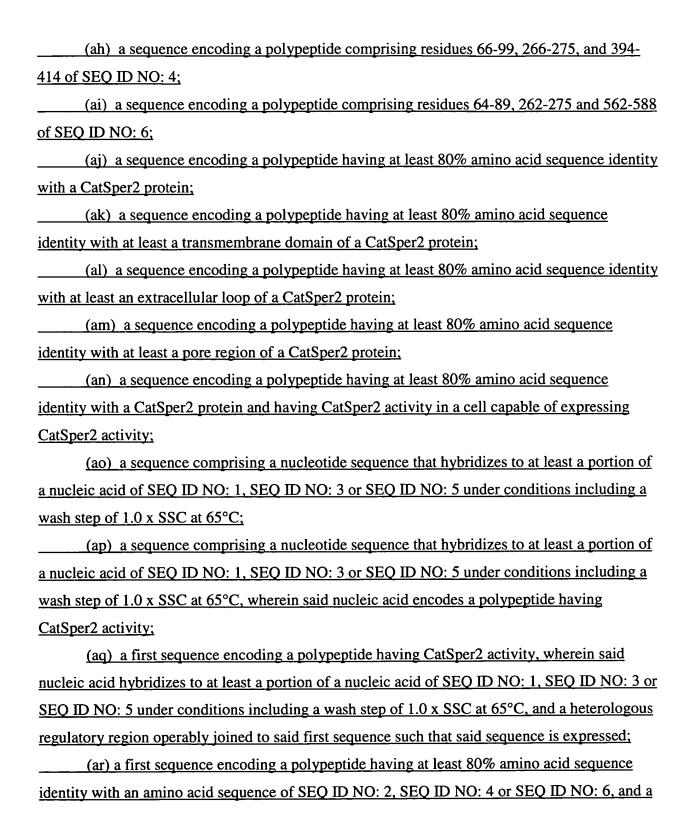


(b) at least 12 consecutive nucleotides of SEQ ID NO: 1;
(c) at least 14 consecutive nucleotides of SEQ ID NO: 1;
(d) at least 16 consecutive nucleotides of SEQ ID NO: 1;
(e) at least 18 consecutive nucleotides of SEQ ID NO: 1;
(f) at least 10 consecutive nucleotides of SEQ ID NO: 3;
(g) at least 12 consecutive nucleotides of SEQ ID NO: 3;
(h) at least 14 consecutive nucleotides of SEQ ID NO: 3;
(i) at least 16 consecutive nucleotides of SEQ ID NO: 3;
(j) at least 18 consecutive nucleotides of SEQ ID NO: 3;
(k) at least 10 consecutive nucleotides of SEQ ID NO: 5;
(1) at least 12 consecutive nucleotides of SEQ ID NO: 5;
(m) at least 14 consecutive nucleotides of SEQ ID NO: 5;
(n) at least 16 consecutive nucleotides of SEQ ID NO: 5;
(o) at least 18 consecutive nucleotides of SEQ ID NO: 5;
(p) a sequence encoding a CatSper2 protein;
(q) a sequence encoding at least a transmembrane domain of a CatSper2 protein;
(r) a sequence encoding at least an extracellular loop of a CatSper2 protein;
(s) a sequence encoding at least a pore region of a CatSper2 protein;
(t) a sequence encoding at least an epitope of a CatSper2 protein having high predicted
antigenicity;
(u) a sequence encoding SEQ ID NO: 2;
(v) a sequence encoding SEQ ID NO: 4;
(w) a sequence encoding SEQ ID NO: 6;
(x) a sequence encoding a polypeptide comprising residues 104-126, 146-166, 176-195,
206-228, 241-262, and 316-340 of SEQ ID NO: 2;
(y) a sequence encoding a polypeptide comprising residues 104-126, 146-166, 176-195,
206-228, 241-262, and 316-340 of SEQ ID NO: 4;
(z) a sequence encoding a polypeptide comprising residues 102-124, 144-164, 174-193,
204-227, 239-260, and 314-338, of SEO ID NO: 6:





(m) at least 14 consecutive nucleotides of SEQ ID NO: 5;
(n) at least 16 consecutive nucleotides of SEQ ID NO: 5;
(o) at least 18 consecutive nucleotides of SEQ ID NO: 5;
(p) a sequence encoding a CatSper2 protein;
(q) a sequence encoding at least a transmembrane domain of a CatSper2 protein;
(r) a sequence encoding at least an extracellular loop of a CatSper2 protein;
(s) a sequence encoding at least a pore region of a CatSper2 protein;
(t) a sequence encoding at least an epitope of a CatSper2 protein having high predicted
antigenicity;
(u) a sequence encoding SEQ ID NO: 2;
(v) a sequence encoding SEQ ID NO: 4;
(w) a sequence encoding SEQ ID NO: 6;
(x) a sequence encoding a polypeptide comprising residues 104-126, 146-166, 176-195,
206-228, 241-262, and 316-340 of SEQ ID NO: 2;
(y) a sequence encoding a polypeptide comprising residues 104-126, 146-166, 176-195,
206-228, 241-262, and 316-340 of SEQ ID NO: 4;
(z) a sequence encoding a polypeptide comprising residues 102-124, 144-164, 174-193,
204-227, 239-260, and 314-338 of SEQ ID NO: 6;
(aa) a sequence encoding a polypeptide comprising residues 127-145, 196-205, and 263-
315 of SEQ ID NO: 2; (ab) a sequence encoding a polypeptide comprising residues 127-145, 196-205, and 265-
315 of SEQ ID NO 4;
(ac) a sequence encoding a polypeptide comprising residues 125-143, 194-203, and 261-
313 of SEQ ID NO 6;
(ad) a sequence encoding a polypeptide comprising residues 280-303 of SEQ ID NO: 2;
(ae) a sequence encoding a polypeptide comprising residues 280-303 of SEQ ID NO: 4;
(af) a sequence encoding a polypeptide comprising residues 278-301 of SEQ ID NO: 6;
(ag) a sequence encoding a polypeptide comprising residues 266-275, 386-400, 447-458,
and 482-494 of SEO ID NO: 2;



heterologous regulatory region operably joined to said first sequence such that said first sequence is expressed; and

(as) a sequence complementary to any one of the sequences of (a)-(ar).

23. (Currently amended) A cell as in claim 22 wherein said nucleic <u>acid</u> is operably joined to heterologous coding sequences to encode a fusion protein.

24. (Original) A cell as in claim 22 wherein said cell is selected from the group consisting of bacterial cells, yeast cells, insect cells, nematode cells, amphibian cells, rodent cells, and human cells.

25. (Original) A cell as in claim 22 wherein said cell is selected from the group consisting of mammalian somatic cells, fetal cells, embryonic stem cells, zygotes, gametes, germ line cells and transgenic animal cells.

26. (Original) A non-human transgenic animal, wherein a genetic construct has introduced a modification into a genome of said animal, or an ancestor thereof, and wherein said modification is selected from the group consisting of insertion of a nucleic acid encoding at least a fragment of a CatSper2 protein, inactivation of an endogenous CatSper2 gene, and insertion by homologous recombination of a reporter gene operably joined to CatSper2 regulatory elements.

27. (Canceled)

28. (Canceled)

29. (Original) A substantially pure protein preparation comprising a polypeptide selected from the group consisting of:

(a) a CatSper2 protein;

(b) at least a transmembrane domain of a CatSper2 protein;

- (c) at least an extracellular loop of a CatSper2 protein;
- (d) at least a pore region of a CatSper2 protein; and
- (e) at least an epitope of a CatSper2 protein having high predicted antigenicity.
- 30. (Amended) A substantially pure protein preparation as in claim 29 wherein said polypeptide is comprises an amino acid sequence selected from the group consisting of:
  - (a) SEQ ID NO: 2;
  - (b) SEQ ID NO: 4;
  - (c) SEQ ID NO: 6;
- (d) residues 104-126, 146-166, 176-195, 206-228, 241-262, and 316-340 of SEQ ID NO: 2;
- (e) residues 104-126, 146-166, 176-195, 206-228, 241-262, and 316-340 of SEQ ID NO: 4;
- (f) residues 102-124, 144-164, 174-193, 204-227, 239-260, and 314-338 of SEQ ID NO: 6;
  - (g) residues 127-145, 196-205, and 263-315 of SEQ ID NO: 2;
  - (h) residues 127-145, 196-205, and 265-315 of SEQ ID NO 4;
  - (i) residues 125-143, 194-203, and 261-313 of SEQ ID NO 6;
  - (j) residues 280-303 of SEQ ID NO: 2;
  - (k) residues 280-303 of SEQ ID NO: 4;
  - (1) residues 278-301 of SEQ ID NO: 6;
  - (m) residues 266-275, 386-400, 447-458, and 482-494 of SEQ ID NO: 2;
  - (n) residues 66-99, 266-275, and 394-414 of SEQ ID NO: 4; and
  - (o) residues 64-89, 262-275 and 562-588 of SEQ ID NO: 6.
- 31. (Currently amended) A substantially pure protein preparation comprising a polypeptide comprising an amino acid sequence having at least 80% amino acid sequence identity with the amino acid sequence of a polypeptide selected from the group consisting of:
  - (a) a CatSper2 protein;

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- (b) at least a transmembrane domain of a CatSper2 protein;
- (c) at least an extracellular loop of a CatSper2 protein; and
- (d) at least a pore region of a CatSper2 protein.
- 32. (Currently amended) A substantially pure protein preparation comprising a polypeptide comprising an amino acid sequence having at least 80% amino acid sequence identity with the amino acid sequence of a CatSper2 protein and having CatSper2 activity in a cell capable of expressing CatSper2 activity.
- 33. (Original) A substantially pure antibody preparation comprising an antibody raised against a CatSper2 epitope.
- 34. (Original) A substantially pure antibody preparation as in claim 33 wherein said epitope has high predicted antigenicity.
- 35. (Currently amended) A substantially pure antibody preparation as in claim 33 wherein said epitope comprises an amino acid sequence within the an amino acid sequence selected from the group consisting of residues 266-275, 386-400, 447-458, and 482-494 of SEQ ID NO: 2, residues 66-99, 266-275, and 394-414 of SEQ ID NO: 4, and residues 64-89, 262-275 and 562-588 of SEQ ID NO: 6.
- 36. (Currently amended) A substantially pure antibody preparation as in any one of claims 33-35 claim 33 wherein said antibody is a monoclonal antibody.
- 37. (Currently amended) A substantially pure antibody preparation as in any one of claims 33-35 claim 33 wherein said antibody is an antibody fragment selected from the group consisting of an Fab fragment, an F(ab')<sub>2</sub> fragment, an Fv fragment, and a single-chain Fv fragment (scFv).

- 38. (Currently amended) A kit for detecting at least an epitope of a CatSper2 protein comprising an anti-CatSper2 antibody of any one of claims 33-37 claim 33 and a means for detecting said antibody.
- 39. (Original) A kit as in claim 38 wherein said means for detecting said anti-CatSper2 antibody comprises a detectable label bound thereto.
- 40. (Original) A kit as in claim 38 wherein said means for detecting said anti-CatSper2 antibody comprises a labeled secondary antibody which specifically binds to said anti-CatSper2 antibody.
- 41. (Original) A method of identifying a potential modulator of CatSper2 activity comprising:

contacting a candidate compound with a cell expressing a CatSper2 protein; measuring an indicator of CatSper2 activity in said cell;

determining whether said candidate compound caused an increase or decrease in said indicator relative to a reference level; and

identifying said candidate compound as a potential modulator of CatSper2 activity if said compound causes an increase or decrease in said indicator.

- 42. (Original) A method as in claim 41 wherein said indicator is an indicator of the level of mRNA encoding said CatSper2 protein.
- 43. (Original) A method as in claim 41 wherein said indicator is an indicator of the level of CatSper2 protein.
- 44. (Original) A method as in claim 41 wherein said indicator is an indicator of cation flux across a membrane of said cell.

- 45. (Original) A method as in claim 41 wherein said indicator is an indicator of whole cell or channel currents of said cell.
- 46. (Currently amended) A method as in any one of claims 41-45 claim 41 wherein said cell has been transformed with a genetic construct which expresses a CatSper2 protein.
- 47. (Original) A method as in claim 41 wherein said cell is a mature sperm cell and said indicator is a measure of sperm motility.
- 48. (Original) A method of identifying a potential modulator of CatSper2 activity comprising:

contacting under physiological conditions a candidate compound with a CatSper2 moiety comprising at least a structural domain of a CatSper2 protein;

measuring binding, if any, between said candidate compound and said CatSper2 moiety; and

identifying said candidate compound as a potential modulator of CatSper2 activity if said candidate compound binds to said CatSper2 moiety.

- 49. (Original) A method as in claim 48 wherein said CatSper2 moiety is a polypeptide selected from the group consisting of:
  - (a) a CatSper2 protein;
  - (b) at least a transmembrane domain of a CatSper2 protein;
  - (c) at least an extracellular loop of a CatSper2 protein; and
  - (d) at least a pore region of a CatSper2 protein.
- 50. (Original) A method of decreasing the fertility of a male subject comprising: administering to said male a compound which decreases CatSper2 activity.

- 51. (Original) A method of causing reversible infertility in a male subject comprising: administering to said male a compound which decreases CatSper2 activity.
- 52. (Canceled)
- 53. (Original) A method of contraception comprising: administering to a female subject a compound which decreases CatSper2 activity.
- 54-60. (Canceled)
- 61. (Original) Use of a compound which decreases CatSper2 activity in the preparation of a medicament for decreasing the fertility of a male subject.
- 62. (Canceled)
- 63. (Canceled)
- 64. (Original) Use of a compound which decreases CatSper2 activity in the preparation of a contraceptive for administration to a female.
- 65-71. (Canceled)
- 72. (Original) A contraceptive preparation comprising a compound which decreases CatSper2 activity.
- 73-74. (Canceled)
- 75. (Original) A method of diagnosing a CatSper2-related disorder in a mammal comprising determining the presence or absence of a mutation in a CatSper2 gene.

76-85. (Canceled)

86. (Original) A method of genotyping a subject with respect to a CatSper2 gene comprising:

determining at least a portion of a CatSper2 gene sequence and comparing said determined sequence to a reference sequence;

wherein the presence or absence of differences between said determined sequence and said reference sequence indicate the presence or absence of a genotype corresponding to said reference sequence.

87-88. (Canceled)

89. (Original) A method of *in vitro* fertilization by sperm having decreased CatSper2 activity comprising:

removing a zona pellucida from at least one ovum; contacting said ovum with at least one of said sperm; and allowing said sperm to fertilize said ovum.

90-91. (Canceled)

92. (Original) A method of treating a subject characterized by infertility due to decreased CatSper2 activity comprising:

transforming sperm or sperm progenitors of said subject with a genetic construct capable of expressing a CatSper2 protein; and

using transformed sperm of said subject to fertilize an ovum.

93. (Canceled)

94. (Original) A method of diagnosing an anti-CatSper2 antibody-mediated infertility caused by anti-CatSper2 antibodies present in a female urogenital tract comprising:

obtaining a sample of antibodies present in a female urogenital tract; contacting said sample of antibodies with at least a fragment of a CatSper2 protein; detecting binding between said sample of antibodies and said fragment of a CatSper2 protein; and

diagnosing an anti-CatSper2 antibody-mediated infertility if binding is detected between said sample of antibodies and said fragment of a CatSper2 protein.

95-100. (Canceled)

- 101. (Original) A method of conducting a drug discovery business comprising:
- (a) identifying, by the assay of claim 41, one or more agents which antagonize CatSper2 activity;
- (b) determining if an agent identified in step (a), or an analog thereof, inhibits at least one of sperm motility or egg penetrance;
- (c) conducting therapeutic profiling of an agent identified as an inhibitor in step (b) for efficacy and toxicity in one or more animal models; and
- (d) formulating a pharmaceutical preparation including one or more agents identified in step (c) as having an acceptable therapeutic profile.

102-111. (Canceled)